

CENTER FOR DRUG EVALUATION AND RESEARCH

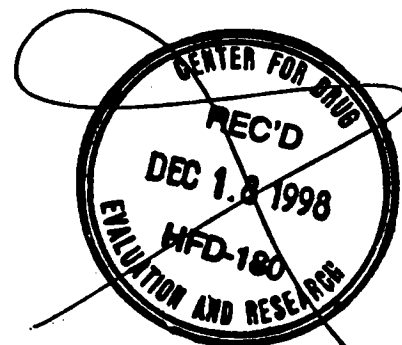
APPLICATION NUMBER: 020698

ADMINISTRATIVE/CORRESPONDENCE DOCUMENTS

LABORATORIES, INC
Braintree

December 17, 1998

Alice Kacuba
Food and Drug Administration
Division of Gastrointestinal and Coagulation
Drug Products (HFD-180)
Document Control Room 6B-24
5600 Fishers Lane
Rockville, MD 20857



Re.: NDA 20-698, MiraLax® (Polyethylene Glycol 3350, NF Powder)

Dear Ms. Kacuba:

Enclosed please find three complete copies of Braintree Laboratories' response to the December 3, 1998 Approvable Letter for its MiraLax NDA.

In addition to those requested in the Approvable Letter, several minor editorial changes have been made to the batch records. In the [REDACTED] batch record, on the first page, under the item section the words "851 Laxative" have been replaced with the product name "MiraLax." In the Braintree Laboratories batch record, "Product 851" has been replaced with "MiraLax"; a line has been added for sign-off on the reproduction of the batch record; and minor format changes have been made.

Also enclosed are three copies of revised draft labeling for container labels, Package Insert and Patient Information. This labeling reflects the agreements reached between Braintree and FDA in the December 11, 1998 teleconference. Additionally, a disk (Word format) contains the Package Insert and Patient Information section.

If you have any questions, please call me or Mark Cleveland.

Sincerely,

Vivian A. Caballero
Director, Regulatory Affairs

cc:

Murray Lumpkin, M.D.
Deputy Center Director for Review Management
Food and Drug Administration CDER (HFD-2)
1451 Rockville Pike
Rockville, MD 20852-1420



NDA 20-698

Food and Drug Administration
Rockville MD 20857

Braintree Laboratories, Inc.
Attention: Mark vB. Cleveland, Ph.D.
60 Columbian Street, P.O. Box 850929
Braintree, MA 02189-0929

DEC - 3 1998

Dear Dr. Cleveland:

Please refer to your new drug application (NDA) dated February 26, 1996, received February 28, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for MirLax® (polyethylene glycol 3350, NF) Powder.

We acknowledge receipt of your submissions dated June 2, August 12, and September 30, 1998.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit an adequate response to our December 2, 1998 letter requesting additional chemistry information.

In addition, it will be necessary for you to submit final printed labeling (FPL) for the drug. The labeling should be identical in content to the enclosed labeling for the package insert and the patient package insert. The final printed labeling for the immediate container labels should be identical to that submitted February 26, 1996, revised as follows:

1. Delete the bolded line under MiraLax.
2. Revise the fifth point under DIRECTIONS to state: "Treatment for 2 to 4 days may be required to produce a bowel movement."
3. Revise the storage statement to be consistent with that requested in the package insert.
4. Revise the CAUTION statement to say "Rx only."

Please submit 20 copies of the final printed labeling, ten of which are individually mounted on heavy weight paper or similar material.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the

application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed. The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, contact Alice Kacuba, Consumer Safety Officer, at (301)827-7310.

Sincerely,

/s/

Lilia Talarico, M.D.

Director

Division of Gastrointestinal

and Coagulation Drug Products

Office of Drug Evaluation III

Center for Drug Evaluation and Research

Enclosures

APPEARS THIS WAY ON ORIGINAL

McNeil

NDA 20-698

Braintree Laboratories, Inc.
Attention: Mark Cleveland, Ph.D.
60 Columbian Street, P.O. Box 850929
Braintree, MA 02185-0929

FEB 24 1997

Dear Dr. Cleveland:

Please refer to your new drug application dated February 26, 1996, received February 28, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Miralax[®] (polyethylene glycol 3350, NF) for Oral Solution.

We acknowledge receipt of your submissions dated April 3, 12, 18, and 23, May 9, 10, 13, 16, and 17, August 30, 1996, January 14 and 16, 1997. The User Fee goal date for this application is February 28, 1997.

We have completed our review and find the information presented is inadequate, and the application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). The deficiencies may be summarized as follows:

1. Clinical:

Studies 851-3, 851-4, 851-5, and 851-6 were submitted in support of the safety and efficacy of the drug for the treatment of occasional constipation.

Study 851-3 was a single center study which randomized 51 constipated patients to a first period (10 days) of either 17 gm or 34 gm of polyethylene glycol (PEG) therapy. Subsequently, and without a washout interval, subjects were randomized to second or third periods of placebo or the alternative PEG dose. An analysis, adjusted for carryover effect from the first 10 day period, of the proportion of successes in all subjects treated with PEG 17 or 34 gm compared to placebo did not demonstrate a significant difference ($p=0.15$ and $p=1.0$, respectively).

Study 851-4 was a nursing home study identical in design to study 851-3. Four patients treated with 17 or 34 gm of PEG experienced profuse diarrhea. The study was discontinued early with no significant difference found for the drug at reduced doses of 6 or 12 gm versus placebo for the 17 patients who completed the protocol.

Study 851-5 was a single-center, randomized crossover study in 25 patients. Analysis of the first one month period before the crossover failed to show any difference between PEG and placebo.

Study 851-6 enrolled 151 subjects randomized to placebo or PEG 17 gm. There was an interim analysis mid-trial. The trial was stopped after a second look at the results, before completing the prospectively established 200 subject sample size. In view of

NDA 20-698

Page 2

these interim looks, the significance was adjusted to $p=0.018$. Analysis of the intent-to-treat population for week one of therapy demonstrated no significant difference in successes comparing PEG 17 gm to placebo. The comparison between PEG 17 gm and placebo for week two of treatment did show a significant difference in favor of the PEG 17 gm over placebo. However, the blinding protection for this study was deficient in that placebo was a sugar water solution. The same sugar, i.e., dextrose, was not part of the PEG solution.

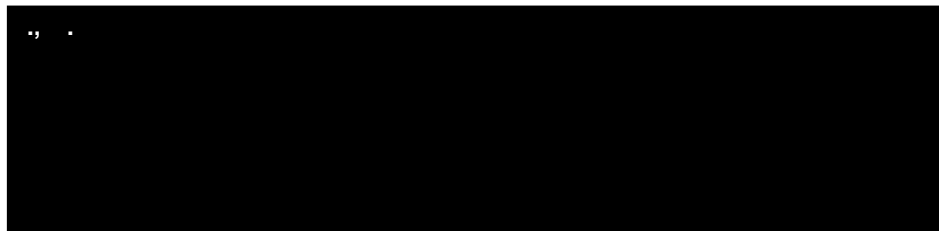
In considering the data provided to demonstrate efficacy, study 851-6 provided some support for the 17 gm dose, but only for the second week of therapy. At least one additional robust, adequate and well-controlled study of the 17 gm dose would be necessary to corroborate this evidence.

As to safety, the excessive diarrhea observed in elderly patients who received 17 or 34 gm of PEG in study 851-4 raises concern as to the compound's safety for use as a laxative in the elderly or pediatric populations. Additional safety data at recommended doses would be needed to adequately characterize the risk of the drug.

2. Chemistry, Manufacturing, and Controls:

A. Drug Master Files (DMFs):

The following DMFs have been found inadequate to support approval, and the DMF holders will be notified of the specific deficiencies:



B. Apparent inconsistencies between procedures and practices at Braintree Laboratories relative to those at [REDACTED]

1. Please provide a specific procedure, i.e. a standard operating procedure (SOP), for the [REDACTED] identification test, for the incoming raw material (PEG 3350 NF) as it is performed at [REDACTED]. An SOP for the [REDACTED] procedure at Braintree Laboratories has been provided, in Volume 1.1.2, pg. 379.
2. The Braintree Laboratories manufacturing documents specify three package sizes for this product: 7, 14, and 26 oz. [REDACTED] bottles, all with child-resistant closures. According to the batch record of the lot from Braintree used for stability studies (Lot D5K001RD), the 128 gm package weight will be filled into the 7 oz. bottle, the 255 gm weight into the 14 oz. bottle, and the 527 gm

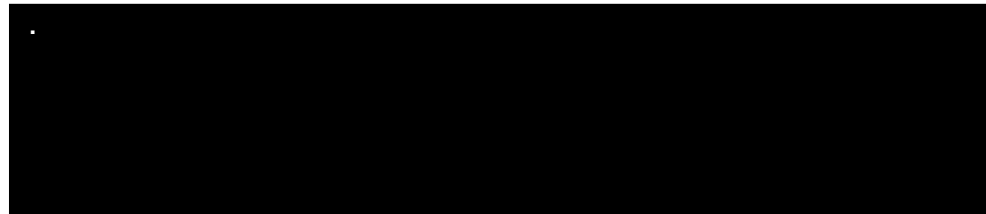
NDA 20-698

Page 3

weight into the 26 oz. bottle. This correlation of these package sizes with these package weights should be explicitly noted on all the production documents, particularly the Master Manufacturing and Production Records, of both facilities.

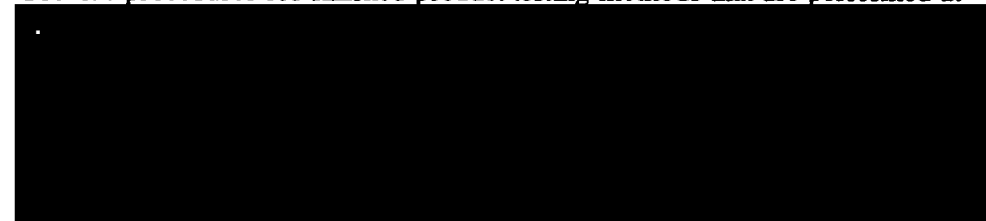
3. A table of contents, which provides a specific title or purpose for each component document, should be included in the manufacturing/production records used by Braintree Laboratories.

- 4.

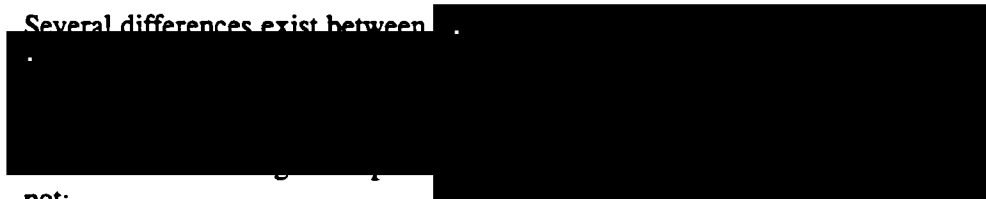


5. Submit a schematic diagram of the production/packaging process as it occurs at the Braintree Laboratories facility. Please describe all equipment and surfaces that contact the drug product, in addition to any cleaning or other preparatory process for the drug product containers.

6. Provide procedures for finished product testing methods that are performed at



7. Several differences exist between



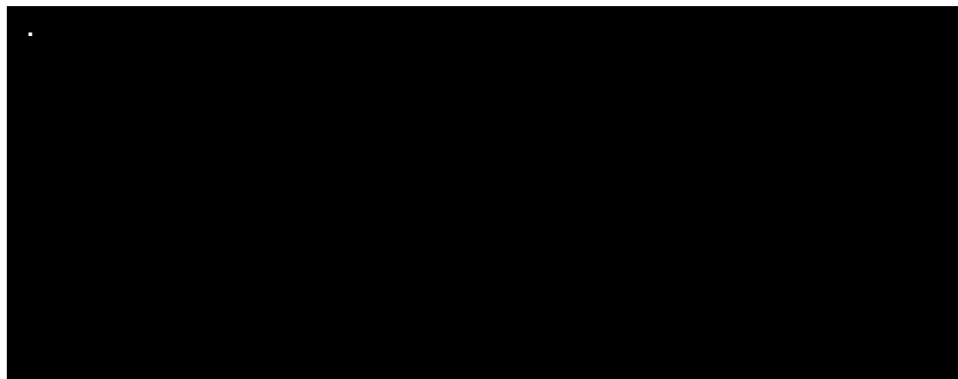
not:

- a.

- b.

- c.

- d.



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These differences should be reconciled such that one set of specifications, which will be used at both facilities, exists for the testing of packaging components.

8. Please provide documents used at Braintree Laboratories which describe the procedures and equipment used in the [REDACTED] test manual and automatic procedures. This information has been provided for [REDACTED] Laboratories in Volume 2 of the initial submission on pp. 238-246 and 247-282, respectively.
9. The certificates of analysis for stability samples analyzed at Braintree Laboratories (for example, Volume 1.1.1, pg. 372) do not contain the identification test, while those from [REDACTED] do. Please provide an explanation regarding exactly what tests are performed as part of the analysis of stability.

C. Facilities cited in the application that will perform either the manufacturing functions or the QC testing for the drug product.

Please describe exactly what the function of each external testing laboratory, listed in Volume 1.1.1, pg. 60, will be.

D. Sampling procedures for the drug substance and packaging components:

1. Please provide information which describes how samples of the finished product are taken for analysis. This information should include how many units per batch are procured for analysis and a description of what method is used to select the units that are to be tested as samples. The statistical basis for the sampling plan should be explained.
2. Please specify how shipments of packaging components (both bottles and caps) are received, the size of a typical shipment, and how the components are sampled for testing. If a procedure such as [REDACTED] is used for this purpose, it should be described in detail.

E. Drug Product Packaging Components, Testing Procedures, and Specifications:

1. For each set of Standard Packaging Instructions used at [REDACTED] an equipment schematic diagram is provided where the processing/packaging is diagrammed. Two of the component parts of this process are the [REDACTED]. This equipment, along with its operation, should be described in detail. Describe the product contact surfaces of the [REDACTED] and in addition, describe the process by which the

NDA 20-698

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containers are [REDACTED] specifically the way they are [REDACTED]

2. In the drawings of the packaging components that are included with the forms for testing of the packaging components that are used at Braintree Laboratories.

3. Please submit a full description of the drug product package, explicitly indicating what material each component part is made from and from what supplier the material is obtained. DMF references for the suppliers should be provided wherever possible.

4. [REDACTED]

F. Drug Product Stability:

1. Regarding the degradation of the drug substance/product, please determine what possible species the drug substance/product could degrade to under stress and/or over time. In addition, please evaluate whether the assay method described is adequate to separate and to determine individually any possible degradation species from the drug substance/product.
2. The submitted stability data is insufficient to support the proposed two year expiry period. Please provide additional stability data, which has been appropriately statistically analyzed. See the following Internet address for further instructions:

[gopher://cdvs2.cder.fda.gov:70/11GOPHER_ROOT%3A%5Bstab%5D](http://cdvs2.cder.fda.gov:70/11GOPHER_ROOT%3A%5Bstab%5D)

3. Regarding data collected at [REDACTED]
 - a. Please specify the humidity of the chamber used to conduct the [REDACTED] stability study. Please note that the ICH-Q1A *Guideline for Industry for the Stability Testing of New Drug Substances and Products* (dated September 1994³) states that long term testing conditions should be $25^{\circ}\text{C} \pm 2^{\circ}\text{C}/60\% \text{ RH} \pm 5\%$.

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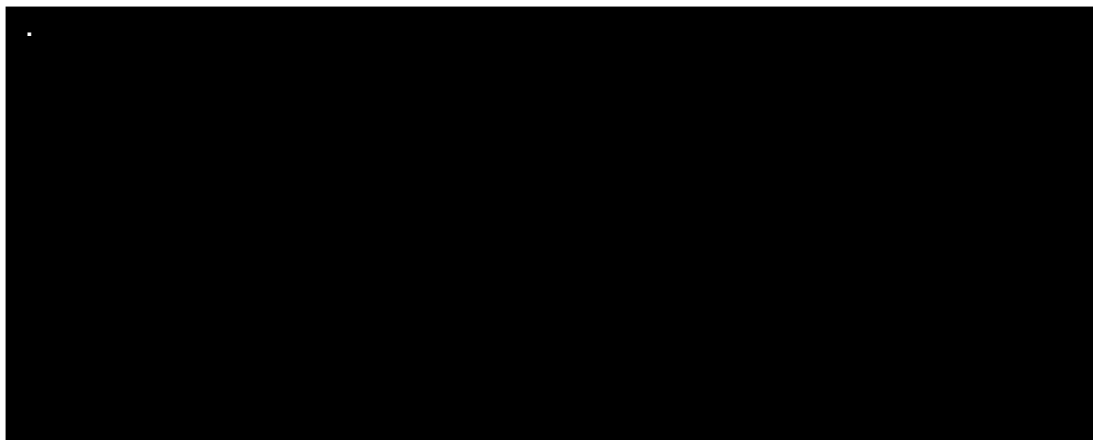
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- b. Please clarify why there are two samples of each package size being studied at [REDACTED] while there is only one sample of each package size kept at the other two sets of conditions.
- 4. Regarding the data collected at Braintree Laboratories:
 - a. Please clarify why the long-term storage conditions were [REDACTED], while stability studies at [REDACTED]. Please specify the [REDACTED] used to conduct the [REDACTED] stability study. Please note that the ICH-Q1A *Guideline for Industry for the Stability Testing of New Drug Substances and Products* (dated September 1994[†]) states that long term testing conditions should be $25^{\circ}\text{C} \pm 2^{\circ}\text{C}/60\% \text{ RH} \pm 5\%$.
 - b. Please state whether the samples were stored in upright or inverted positions.
- 5. Stability data which was collected using earlier lots of material stored in a different container/closure is provided starting in Volume 1.1.2, pg. 299. Development data such as these from a container/closure system different from that proposed for marketing are not suitable as primary stability data to support the proposed expiry.

G. Regarding the Environmental Assessment:

Sections 4 and 7-11 do not include enough information to evaluate the effect on the environment that the manufacture and marketing of this product will have.

Please refer to the Guidance for Industry for the Submission of an Environmental Assessment in Human Drug Applications and Supplements, released by the Center for Drug Evaluation and Research (CDER) in November 1995[†].

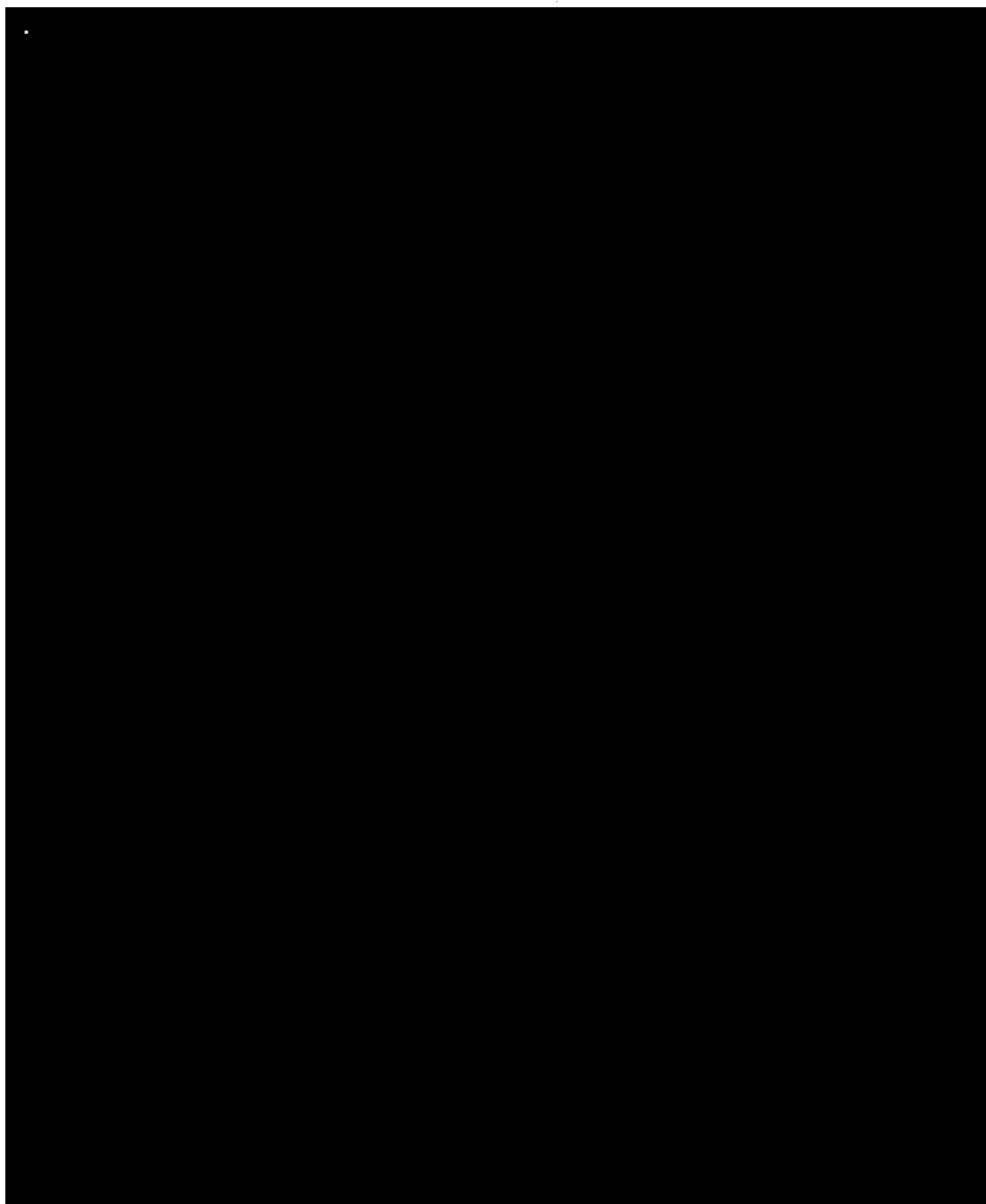


NDA 20-698

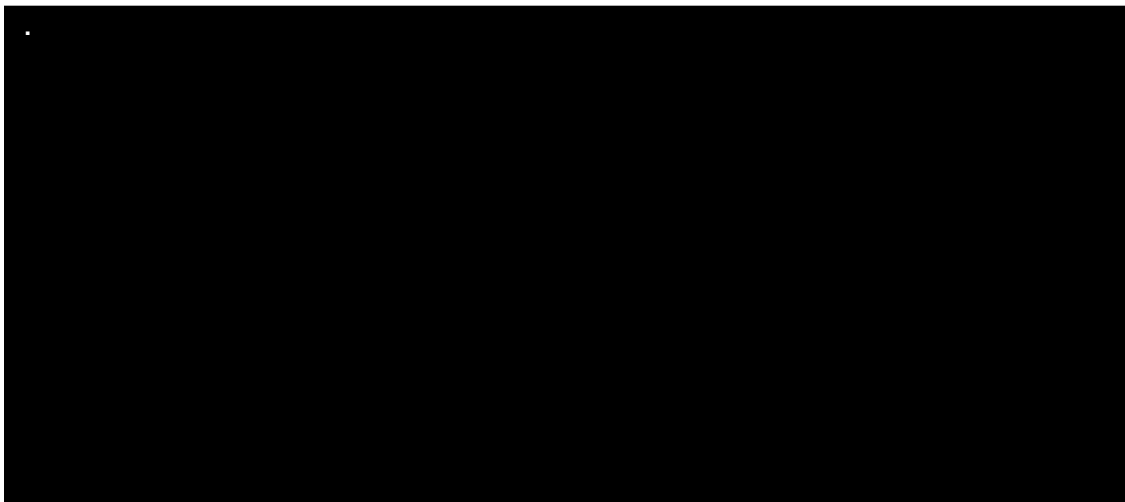
Page 7

H. Validation of the analytical methods used to characterize the drug product:

1. Confirm that other ethoxylates of different molecular weight can be observed by the proposed assay method.



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‡ - Guidances and guidelines referred to in this letter are available in their entirety on the CDER general Internet site. The address of that site is <http://www.fda.gov/cder>. They are also available from the Consumer Affairs Branch, HFD-210, Center for Drug Evaluation and Research, 7500 Standish Place, Rockville, MD 20855, tel. 301-594-1012.

Labeling comments will be forthcoming once the application is otherwise approvable.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the application. Any amendments should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

If you have any questions, please contact Melodi McNeil, Consumer Safety Officer, at (301) 443-0483.

Sincerely yours,

/s/

2/24/97

2/24/97

Stephen B. Fredd, M.D.
Director

Division of Gastrointestinal and Coagulation
Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Division of Gastrointestinal & Coagulation Drug Products

CONSUMER SAFETY OFFICER REVIEW

Application Number: 20-698

Name of Drug: MiraLax (polyethylene glycol 3350, NF) Powder

FEB 18 1999

Sponsor: Braintree Laboratories, Inc.

Material Reviewed

Submission Date: February 11, 1999

Receipt Date: February 12, 1999

Background and Summary Description: NDA 20-698, was submitted on February 26, 1996, for the treatment of occasional constipation. A Not Approvable (NA) action was taken on February 24, 1997 due to clinical and chemistry deficiencies. On June 3, 1998, the firm submitted a complete response to the NA letter for which an Approvable (AE) letter was issued December 3, 1998, pending chemistry and labeling deficiencies. A teleconference was held with the firm on December 11, 1998, to finalize the labeling; revised draft labeling was submitted December 17, 1998, and Final Printed Labeling (FPL) was submitted on February 11, 1999. The CMC review recommends that the application be approved.

Review

The FPL was compared to the labeling submitted December 17, 1998 (See Consumer Safety Officer Review dated January 28, 1999). Comments pertain to both the 527 gram bottle and the 255 gram bottle.

The firm corrected the typographical error (involving the chemical formula) in the DESCRIPTION section.

Other revisions were:

1. [REDACTED] has been added to the bottle label. This revision is supported by patent information submitted by the firm on February 8, 1999 and is acceptable.
2. On the bottle label, the statement "Store at 25° C (77° F)" has been repositioned to make room for a bar code. These revisions are editorial and are acceptable.

3. The PATIENT INFORMATION sheet and the package insert are printed as a single continuous sheet of paper which is attached to the bottle label and can be separated from the bottle. The manner in which it is printed prevents the two documents from being separated into two separate documents; one of which is given to the patient. The firm should be notified to resolve this at the next printing of the FPL.

Conclusions

The February 11, 1999 FPL is acceptable. The application should be approved and the firm notified to revise, at the next printing, the tear away PATIENT INFORMATION and package insert to allow for the separation of the documents.

/S/

2-18-99

Alice Kacuba
Consumer Safety Officer

/S/

2/18/99

Kati Johnson
Supervisory Comment/Concurrence:

/S/

2-18-99

Lilia Talarico, M.D.
Division Director

cc:

Original NDA 20-698
HFD-180/Div. Files
HFD-180/A.Kacuba
HFD-180/L.Talarico

Drafted by: A.Kacuba/February 16, 1999/
R/D Initials: K.Johnson/February 17, 1999
Final: A.Kacuba/February 18, 1999
Filename: c:\wpfiles\20-698FPL.doc

CSO REVIEW

APPEARS THIS WAY ON ORIGINAL

CSO/Kacuba

Division of Gastrointestinal & Coagulation Drug Products

CONSUMER SAFETY OFFICER REVIEW

Application Number: NDA 20-698

Name of Drug: MiraLax (polyethylene glycol 3350, NF) Powder

JAN 28 1999

Sponsor: Braintree Laboratories, Inc.

Material Reviewed

Submission Date: December 17, 1998

Receipt Date: December 18, 1998

Background and Summary Description:

NDA 20-698, was submitted on February 28, 1996, for the treatment of occasional constipation. A Not Approvable (NA) was issued on February 24, 1997. On June 3, 1998, the firm submitted a complete response to the NA letter for which an Approvable (AE) letter was issued December 3, 1998, pending chemistry and labeling deficiencies. A telecon was held with the firm on December 11, 1998, to finalize labeling. On December 17, 1998, the firm submitted revised draft labeling.

Review

The revised draft labeling (Attachment A) was compared to the December 3, 1998, AE letter labeling, and the final agreements reached in the December 11, 1998, telecon (Attachment B).

Revisions were made in the package insert, carton label, and the patient information sheet to comply with the December 3, 1998, AE letter and the December 11, 1998, telecon with the firm.

Other revisions were:

1. On the bottle label and on the package insert, the word [REDACTED] preceding the words "Rx only" has been eliminated. These revisions were made to comply with the FDAMA legislation. These revisions are acceptable.
2. On the PATIENT INFORMATION sheet, in the first sentence, the words "polyethylene glycol" have been capitalized. This revision is supported by the chemistry review and is acceptable.
3. On the PATIENT INFORMATION sheet, in the first sentence, the notation [REDACTED] was added after the words "polyethylene glycol". This revision is supported by the chemistry review and is acceptable.
4. On the package insert, in the DESCRIPTION section, the chemical formula has an apparent

typographical error. It reads $\text{HO}(\text{C}_2\text{H}_4\text{O})_n$ and should read $\text{HO}(\text{C}_2\text{H}_4\text{O})_n\text{H}$. This needs to be corrected.

5. On the package insert, in the CLINICAL PHARMACOLOGY section, the first sentence has been revised to read: Essentially, complete recovery of MiraLax was shown in normal subjects without constipation. This revision is editorial and is acceptable.

Conclusions

The December 17, 1998, revised draft labeling is acceptable pending the correction of the typographical error in the DESCRIPTION section. The firm should be notified to submit FPL.

/S/

Alice Kacuba
Consumer Safety Officer

1-25-99

Supervisory Comment/Concurrence:

/S/

Kati Johnson
Supervisory Consumer Safety Officer

1/26/99

/S/

Lilia Talarico, M.D.
Division Director

1-28-99

cc:

Original NDA 20-698
HFD-180/Div. Files
HFD-180/A.Kacuba
HFD-180/Lilia Talarico

APPEARS THIS WAY ON ORIGINAL

drafted: A.Kacuba/January 14, 1999
R/D Initials: K.Johnson/January 20, 1999
final: AK/January 20, 1999
filename: c:\wpfiles\20698-revised-labeling-review-1-13-99.doc

CSO REVIEW

MEMORANDUM OF TELECON

DATE: December 11, 1998

APPLICATION NUMBER: NDA 20-698; Miralax (PEG 3350, NF) Powder for Oral Solution

BETWEEN:

Name: Dr. Mark Cleveland, Vice President, New Product Development
Ms. Vivian Caballero, Director, Regulatory Affairs
Phone: (781) 843-2202
Representing: Braintree Laboratories

AND

Name: Dr. Lilia Talarico, Division Director
Dr. Hugo Gallo-Torres, Medical Team Leader
Ms. Kati Johnson, SCSO
Ms. Alice Kacuba, CSO
Division of Gastrointestinal and Coagulation Drug Products, HFD-180

BACKGROUND: NDA 20-698 was submitted on February 26, 1996 to market Miralax (PEG 3350) Powder for Oral Solution, at a dose of 17 gm, for the treatment of occasional constipation. A Not Approval (NA) letter was issued on February 24, 1997 informing the firm of clinical and chemistry deficiencies. Subsequently, meetings were held with representatives from the firm, the Division, and the Office to discuss the NA letter. On June 2, 1998, the firm submitted a complete response to the NA letter. An approvable (AE) letter was issued on December 3, 1998. (pending labeling and chemistry deficiencies.) On December 3, 1998, Dr. Cleveland and Ms. Caballero called me to discuss numerous issues regarding the labeling revisions that we requested in the December 3, 1998 AE letter. A telecon was scheduled to finalize the labeling. In preparation for this telecon, the firm faxed the proposed revisions to the Agency on December 9, 1998, and followed it up by submitting a hardcopy to the application (See attached).

TODAY'S PHONE CALL: The Agency addressed the firm's seven proposed revisions in the labeling.

1. The Agency accepted the firm's proposal to retain the statement "Patients taking other medications containing polyethylene glycol have occasionally developed urticaria suggestive of an allergic reaction" in the ADVERSE REACTIONS section of the package insert.
2. The Agency accepted the firm's proposal of moving the bolded colored line from under the word MiraLax to under the generic name in place of removing the line from the label.
3. The AE labeling removed the phase [REDACTED] from the PRECAUTIONS, the DOSAGE AND ADMINISTRATION, and the HOW SUPPLIED sections of the package insert as well as from the "How to Take" section of the PATIENT INFORMATION label. Since the primary support for demonstration of efficacy was a study in which the drug was

taken with water, the firm's proposal to reintroduce the words [REDACTED] was not accepted.

4. The December 3, 1998 AE letter added a statement to the PRECAUTIONS DRAFT LABELING [REDACTED]

5. The Agency accepted the firm's proposal to retain the statement "There is no evidence of tachyphlaxis" in the CLINICAL PHARMACOLOGY, "Pharmacology" section of the package insert.

6. The firm proposes that the "Geriatric Use" section read DRAFT LABELING [REDACTED]

should be discontinued".

7. The firm was directed to retain the wording proposed in the December 3, 1998 AE letter.

The firm agreed to submitting draft labeling incorporating these changes, along with addressing the chemistry deficiencies stated in the December 2, 1998 IR letter. The call was concluded.

Alice Kacuba
Consumer Safety Officer

cc: Original

HFD-180/Div. File

HFD-180/L.Talarico

HFD-180/H.Gallo-Torres

HFD-180/A.Kacuba

drafted: A.Kacuba/December 18, 1998

R/D initialed by: K.Johnson/January 9, 1999

final: AK/January 11, 1999

filename: c:\mydocuments\NDA20698-AE-labeling-questions-from-firm

TELECON

APPEARS THIS WAY ON ORIGINAL [REDACTED]

LABORATORIES, INC
BrainTree

December 9, 1998

Alice Kacuba
Food and Drug Administration
Division of Gastrointestinal Drug Products (HFD-180)
Document Control Room 6B-24
5600 Fishers Lane
Rockville
MD 20857

Re: NDA 20-698 MiraLax®

Dear Ms. Kacuba:

As requested today by Kati Johnson, I have enclosed a list of questions and some proposed wording pertaining to the revised MiraLax labeling which FDA provided with the December 3, 1998 Approvable Letter. I have also enclosed a marked up label copy with suggested changes indicated.

As I discussed yesterday with Dr. Talarico, scheduling of a teleconference as soon as possible will help in clarifying these points so that we may submit our response to the Approvable Letter. Please contact me or Vivian Caballero with the time for the teleconference.

Sincerely,



Mark Cleveland, Ph.D.
Vice President
New Product Development

REQUEST FOR TRADEMARK REVIEW

McNeil
(624)

To: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair (HFD-530), 9201 Corporate Blvd, Room N461

From: Division of Gastrointestinal and Coagulation Drug Products		HFD-180
Attention: Melodi McNeil, CSO		Phone: (301) 443-0483
Date: April 30, 1996		
Subject: Request for Assessment of a Trademark for a Proposed New Drug Product		
Proposed Trademark: Miralax		NDA/ANDA# NDA 20-698
Established name, including dosage form: Polyethylene glycol 3350, NF Powder		
Other trademarks by the same firm for companion products: GoLYTELY, NuLYTELY (PEG 3350, NF plus electrolytes)		
Indications for Use (may be a summary if proposed statement is lengthy): Treatment of occasional constipation.		
Initial Comments from the submitter (concerns, observations, etc.): Note: this application was originally consulted to the nomenclature committee on 3/28/96. However, the consult was canceled when it was discovered that the name proposed by the firm at that time ("851 Laxative") was not the name intended for marketing purposes. The firm proposes to market this as a Rx (prescription) product.		

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

cc: Original NDA 20-698; HFD-180/division file; HFD-180/M.McNeil; HFD-180/RFrankewich

Rev. December 95



Consult #624 (HFD-180)

MIRALAX

(polyethylene glycol 3350 powder)

The LNC found no look alike/sound alike conflicts in the proposed proprietary name. However, the Committee is concerned that the trademark conveys the impression of "miracle laxative" which is fanciful and misleading.

The LNC asks the Division to consider this concern in it's evaluation of the trademark. If the Division feels this is not uncustomary in the type of products submitted then , The LNC will have no reason to find the proposed proprietary name unacceptable.

/S/

6/20/96

, Chair

CDER Labeling and Nomenclature Committee

EXCLUSIVITY SUMMARY FOR NDA # 20-698

SUPPL # _____

Trade Name: MiraLax

Generic Name: Polyethylene Glycol 3350, NF

Applicant Name: Braintree Laboratories, Inc.

HFD # 180

Approval Date If Known _____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it an original NDA?

YES ☒ NO _____

b) Is it an effectiveness supplement?

YES _____ NO ☒

If yes, what type? (SE1, SE2, etc.) _____

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES ☒ NO _____

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

YES _____ NO **X**

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

No

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO-please indicate as such)

YES _____ NO **X**

If yes, NDA # _____. Drug Name _____

3. Is this drug product or indication a DESI upgrade?

YES NO **X**

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES X NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

- NDA# 19-011 GoLYTELY
- NDA# 19-797 NuLYTELY
- NDA# 18-983 Colyte
- NDA# 19-284 OCL

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES ____ NO ____

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

- NDA# _____
- NDA# _____
- NDA# _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES ☒ NO ☐

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES ☒ NO ☐

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES ☐ NO ☒

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES ____ NO ____

If yes, explain: _____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES ____ NO X ____

If yes, explain: _____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Study 851-3; Evaluation of 851 Laxative Solution in Constipated Patients

Study 851-6; Evaluation of 851 Laxative Solution in constipated Patients

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1

YES ____

NO X__

Investigation #2

YES ____

NO X__

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1

YES ____

NO X__

Investigation #2

YES ____

NO X__

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Study 851-3; Evaluation of 851 Laxative Solution in Constipated Patients

Study 851-6; Evaluation of 851 Laxative Solution in Constipated Patients

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # [redacted] YES X NO Explain:

Investigation #2

IND # [redacted] YES X NO Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES Explain NO Explain

Investigation #2

YES Explain NO Explain

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES ____ NO X

If yes, explain: _____

/s/ [Redacted]

2-18-99
Date

Signature
Title: CSO

/s/ [Redacted]

2-18-99
Date

Signature of Office/
Division Director

cc: Original NDA Division File HFD-93 Mary Ann Holovac

APPEARS THIS WAY ON ORIGINAL

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number: 20698 Trade Name: 851 LAXATIVE (PEG 3350.NF)
Supplement Number: _____ Generic Name: 851 LAXATIVE
Supplement Type: _____ Dosage Form: PDR
Regulatory Action: PN Proposed Indication: Constipation

IS THERE PEDIATRIC CONTENT IN THIS SUBMISSION? NO

What are the INTENDED Pediatric Age Groups for this submission?

 NeoNates (0-30 Days) Children (25 Months-12 years)
 Infants (1-24 Months) Adolescents (13-16 Years)

Label Status -
Formulation Status -
Studies Needed -
Study Status -

Are there any Pediatric Phase 4 Commitments in the Action Letter for the Original Submission? NO

COMMENTS:

This Page was completed based on information from a PROJECT MANAGER/CONSUMER SAFETY OFFICER,
ALICE KACUBA/SI

Signature

Date

2-4-99

APPEARS THIS WAY ON ORIGINAL